Developing better biopharmaceuticals using biomolecular simulation and modelling

This project is one of a number that are in competition for funding from the South West Biosciences Doctoral Training Partnership (SWBio DTP) which is a BBSRC-funded PhD training programme in the biosciences, delivered by a consortium comprising the Universities of Bath, Bristol, Cardiff and Exeter, along with the Rothamsted Research Institute. The partnership has a strong track record in advancing knowledge through high quality research and teaching, in collaboration with industry and government.

Studentships are available for entry in September/October 2019.

All SWBio DTP projects will be supervised by an interdisciplinary team of academic staff and follow a structured 4-year PhD model, combining traditional project-focussed studies with a taught first year which includes directed rotation projects.

Lead supervisor: Dr Christopher Pudney, Department of Biology & Biochemistry
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Co-supervisors: Dr Marc van der Kamp (University of Bristol), Prof David Leak
                         (University of Bath)

Non-academic CASE supervisor: Dr David Cole, Immunocore Ltd.

Project description

Most bio-molecular interactions are thought to increase the (local) rigidity of a complex and this paradigm is applied when designing new drugs. However, targeting rare, dynamically interconverting conformers is potentially a pathway to potent and specific drugs. We focus on the Human Leukocyte Antigen (HLA), which plays a crucial role in the adaptive immune system by presenting peptides for recognition by the αβ T cell receptor (TCR). The role that the peptide plays in tuning HLA flexibility during TCR recognition is potentially crucial in determining the functional outcome of an immune response. We have evidence that the recognition peptide is able to modulate the conformational dynamics of the HLA and that these changes are detected by the TCR, reflected by substantial changes in TCR-peptide-HLA binding affinity.

Developing new biopharamceuticals by incorporating information on molecular dynamics is a new paradigm for the design of peptide-based drugs and opens up many new opportunities for therapeutics. Computational simulation is ideally placed explore and predict the potential of new peptide-based drugs incorporating molecular dynamics information. In particular, the use of enhanced sampling methods allows the exploration of very large effective time-scales and this is the key to accurately capturing the molecular dynamics of these systems. Using these approaches, combined with complementary experimental tools, the project will develop the ability to truly provide a rationale design of peptide-based drugs within the HLA-TCR system.

The project is truly cross-disciplinary, incorporating new advances in computational simulation and novel experimental techniques that complement the computational work and the direct involvement of the ideal industrial partner. Moreover, the student will have the advantage of spending time in different research environments (Bath, Bristol and with the industrial partner). The training potential for the student is outstanding and will enable to the successful student to develop their career in a commercially valuable and growing area. We expect the student will attend and present at appropriate national and international conferences as well as interact with industrial level meetings to present work to stakeholders.

Funding

Studentships provide funding for a stipend at the standard UKRI rate (currently £14,777 per annum, 2018/19 rate), research and training costs and UK/EU tuition fees for 4 years.

UK and EU applicants who have been residing in the UK since September 2016 will be eligible for a full award; a limited number of studentships may be available to EU applicants who do not meet the residency requirement. Applicants who are classed as Overseas for tuition fee purposes are not eligible for funding.

Applications

Applicants must have obtained, or be about to obtain, a First or Upper Second Class UK Honours degree, or the equivalent qualifications gained outside the UK, in an appropriate area of science or technology.

Applications should be submitted on the [University of Bath's online application form for a PhD in Biosciences](#). Please ensure that you quote the supervisor's name and project title in the 'Your research interests' section. You may apply for more than one project if you wish but you should submit a separate personal statement relevant to each one.

The deadline for the receipt of applications is Monday 3 December 2018.